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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,704	02/05/2004	George C. Tsokos	Army 178	5604

30951 7590 08/25/2006

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EXAMINER	
SCHULTZ, JAMES	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/772,704	TSOKOS ET AL.	
	Examiner	Art Unit	
	J. D. Schultz, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1, 10, 11, 15, 29 and 30*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,11,15,29 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,11,15,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attached*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 18 May 2006 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 17 January 2006 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 5 February 2004 was filed before the mailing date of first Official action on the merits, mailed 17 January 2006. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner, and a signed and initialed copy is enclosed herewith.

Claim Objections

Claims 10 and 30 are objected to because of the following informalities: "leukopheresing" appears to be a misspelling of "leukophoresing." Appropriate correction is required.

Priority

Priority continues to be denied since the instant specification is considered to be lacking enablement for reasons discussed in detail below. Since the prior document cannot be considered to be enabling for said reasons, the application therefore does not comply with 35 U.S.C. § 112 first paragraph enablement, and cannot be relied upon for priority.

Claim Rejections - 35 USC § 112

Claims 1, 10, 11, 15, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the previous action, the specification does not provide the requisite guidance such that any person skilled on the art would be able to practice the claimed methods without performing undue *de novo* trial and error experimentation. The undue trial and error experimentation stems from the silence of the prior art as it pertains to antisense mediated upregulation of IL-2 in treating lupus, and also to the difficulty of transfecting cells with a high enough concentration of antisense modulator to achieve a therapeutic effect in vivo. While it is apparent that the instant specification and the publication of Tenbrock et al. (as referenced on the Form PTO-1449 filed 9/24/05 with this Application; co-authored by the instant inventor Tsokos) both show that antisense may be used to up regulate IL-2 in vitro, there are only prophetic indications in both of the instant specification and the prior art reference of Tenbrock that such upregulation would lead to the treatment of lupus. There is no apparent evidence from either the

instant specification or the prior art that upregulation of IL-2 would necessarily result in a treatment for lupus, nor have applicants pointed to any such art. Since the state of the art of treating lupus is considered to be generally unpredictable, since few if any effective treatments are found in the prior art, prophetic examples combined with in vitro data are not considered to be reasonably predictive of what would happen in a treatment scenario, because it is held that lupus is a disease of the organ-level physiology of the immune system, which cannot be modeled by an in vitro system, and that therefore, such a system is not representative of treatment of lupus.

Furthermore, the state of the art of the delivery of nucleic acid therapeutics *in vivo* can best be summarized by Tenbrock et al; "electroporation, which was used to insert the antisense plasmid into primary SLE T cells, cannot be used currently in clinical practice."

In response, applicants have argued that the inventors have shown that by expressing the CREM antisense, they can increase the expression of IL-2 mRNA. This discovery is not in doubt by the examiner as it pertains to in vitro results. Rather, the concern is whether or not such IL-2 upregulation can be performed in vivo, and whether such upregulation would lead to a treatment for lupus.

Applicants have also argued that the specification clearly sets forth that the inventors propose to remove lymphocytes, treat the lymphocytes with an antisense construct, and reinfuse the cells into the patient using generic delivery and treatment methods. Applicants assert that such teachings demonstrate that the inventors had possession of the invention. However, the instant rejection is not based on any potential lack of possession. The instant invention is based on whether or not the claim can be predictably practiced given the guidance provided by the

specification in the prior art. Since it has held that neither the specification or the prior art are enabling, the prophetic treatment regimen described above does not render predictable results which would otherwise be in doubt based solely upon the teachings of the instant specification and prior art.

While applicants have asserted that the step of electroporation of the antisense construct into the cells occurs outside the body, and therefore presumably could be practiced ex vivo, it is not clear for the reasons provided above that even if such delivery could be achieved, that treatment of lupus would result. The rejection is maintained therefore.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. D. Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JDS

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER